DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office

60 8th Street, N.E.
Atlanta, Georgia 30309

420 NC-1-35

September 10, 1997

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Robert V. Toni
President/Chief Executive Officer
Closure Medical Corporation
5265 Capital Boulevard
Raleigh, North Carolina 27616

WARNING LETTER

Dear Mr. Toni:

An inspection of your firm was conducted on July 7-28, 1997, by Investigator Claudette D. Brooks. Our investigator found that you currently formulate, test, fill, and package Octyldent, a dental adhesive. Octyldent is a device as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Investigator Brooks documented several significant deviations from the Good Manufacturing Practice for Medical Devices (GMPs) as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 820. These observations would also be violations of the Quality System Regulation, 21 CFR Part 820, which became effective June 1, 1997. These deviations cause the device you manufacture and distribute to be adulterated within the meaning of Section 501(h) of the Act.

You have failed to establish and implement an adequate complaint handling program. Complaints are not received, documented, and evaluated in a timely manner. Complaints received at your primary distributor, [redacted] were not documented by your facility until up to six months after initial receipt. No formalized complaint handling procedures have been established with [redacted] which would address the manner and frequency of forwarding pertinent complaint information to allow for proper evaluation and follow-up. Investigator Brooks was told that complaints are received from [redacted] approximately every three months. Complaints were also noted to routinely remain outstanding for months before Closure initiated any evaluation to determine appropriate follow-up.

The available procedures which addressed the handling of Mandatory Device Reporting (MDR) complaints were inconsistent and provided conflicting instructions. One procedure stated that these complaint reviews were the responsibility of the Product Experience Review Committee, a second procedure stated that the review was the responsibility of the Senior Staff, and a third procedure stated that customer relations would make these determinations. You also failed to follow your reporting procedures for two incidents involving medical intervention. Your MDR reporting responsibilities are described in 21 CFR Part 803.

You have failed to appropriately review, evaluate, and maintain all complaints pertaining to your Octyldent product. You have failed to properly determine whether or not an investigation is necessary. If no investigation was made, you failed to maintain any documentation of the reasons for this decision. Some of these unresolved complaints had been received in January 1997. All complaints involving the possible failure of the device to meet any of its performance specifications must be reviewed, evaluated, and investigated. Investigator Brooks' review of your complaint files revealed that the majority of the complaints did not contain any record of investigation or justification for failure to perform an investigation. Other documentation problems noted in your complaint files included no record of returned sample analysis and no indication of the nature of the complaint. In addition, the complaint files did not routinely include any reply to the complainant or related correspondence when investigations were performed.

Your quality assurance program failed to respond to device quality problems identified as a result of consumer complaints and retained product testing. Your quality assurance program is responsible for identifying, recommending, and providing solutions for quality assurance problems and verifying the implementation of such solutions. You received approximately thirty four complaints on Octyldent, Lot #084069. Seven months after the product was released for distribution, you confirmed by retained sample analysis that the product failed to meet viscosity specifications. No documentation was available indicating any corrective action in response to these complaints that the product could not be used.

You have failed to validate the filling operations for the Octyldent product. You could not provide documented evidence which established a high degree of assurance that the filling procedures in use are effective and could consistently produce a product meeting its predetermined specifications and quality attributes.

You have failed to follow your written procedures for the auditing of vendors. You have not conducted supplier audits as required by your procedures even for vendors you have classified as critical. Your firm had audit information on only seven of approximately [redacted] critical vendors. Only one of the approximately [redacted] major vendors had been audited.

This inspection was initiated in response to the [redacted] were noted pertaining to the [redacted] product. These [redacted] Based on these observations, we have recommended to the Center for Devices and Radiological Health that [redacted]

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. At the close of the inspection, the Inspectional Observations (FDA 483) was issued to and discussed with you. The specific violations noted in this letter and in the FDA 483 are symptomatic of serious underlying problems in your firm's quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

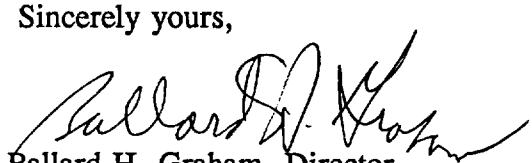
Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submission of devices to which the GMP deficiencies are reasonably related will be cleared until these violations have been corrected. Also, no request for Certificates for Products for Export will be approved until the violations related to the subject device have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory actions being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

If you have any questions regarding this letter or if you desire a meeting with Agency staff to discuss our opinion, contact me or Philip Campbell at (404) 347-3162. We anticipate that you will contact this office about implementation of any corrective action such as the completion of the various validation studies. Any future inspections will be scheduled in response to such correspondence.

Sincerely yours,



Ballard H. Graham, Director
Atlanta District